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(54) **PROCESS FOR PRODUCING QUINAZOLIN-4-ONE AND DERIVATIVE THEREOF**

(57) A process for preparing quinazolin-4-one or its derivative by reacting anthranilic acid or its derivative with formic acid or its derivative in the presence of ammonia, or by reacting ammonium anthranilate or its derivative with formic acid or its derivative.

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Description

FIELD OF THE INVENTION

[0001] The present invention relates to a process for preparing quinazolin-4-one or its derivatives from anthranilic acid or its derivatives or ammonium anthranilate or its derivatives. The quinazolin-4-one and its derivatives are useful as intermediates or starting compounds for preparing pharmaceutically active compounds or agricultural chemicals.

BACKGROUND OF THE INVENTION

[0002] The following processes are known for preparing quinazolin-4-one or its derivatives from anthranilic acid or its derivatives.

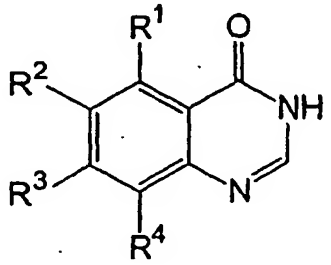
1) EP 1029853 discloses a process for preparing 6-iodoquinazolin-4-one by reacting 5-iodoanthranilic acid with formamidine acetate in ethanol for 20 hours. This process has problems in that the reaction period is long, and it is necessary to use expensive formamidine in an excessive amount.
2) Chem. Pharm. Bull., 46, 1926 (1998) describes a process for preparing quinazolin-4-one by reacting anthranilic acid with formamide. This process has a problem in that teratogenetic formamide is used in an excessive amount.

[0003] Thus, these processes have various problems, and hence are not satisfactory as industrially employable processes for preparing quinazolin-4-one or its derivatives.

SUMMARY OF THE INVENTION

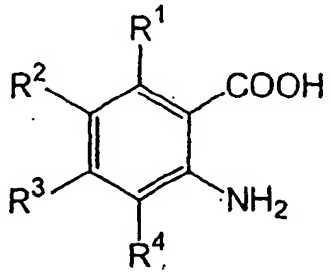
[0004] The present invention has an object to provide an industrially advantageous simple process for preparing quinazolin-4-one or its derivatives from anthranilic acid or its derivatives or ammonium anthranilate or its derivatives in high yields under moderate conditions.

[0005] The present invention resides in a process for preparing quinazolin-4-one or a derivative thereof having the formula (2):



(2)

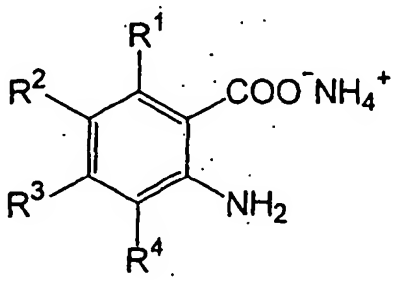
in which each of R^1, R^2, R^3 and R^4 independently represents a hydrogen atom, a halogen atom, or a group that does not participate in the following reaction and may have a substituent, or R^1, R^2, R^3 and R^4 may be combined to form a ring, which is characterized in that an anthranilic acid or a derivative thereof having the formula (1):



(1)

in which each of R^1, R^2, R^3 and R^4 has the same meaning as above,
is reacted with formic acid or a derivative thereof in the presence of ammonia.

[0006] The invention further relates to a process for preparing quinazolin-4-one or a derivative thereof having the above-mentioned formula (2) which is characterized in that ammonium anthranilate or a derivative thereof having the formula (3):



(3)

in which each of R^1, R^2, R^3 and R^4 independently represents a hydrogen atom, a halogen atom, or a group that does not participate in the following reaction and may have a substituent, or R^1, R^2, R^3 and R^4 may be combined to form a ring, is reacted with formic acid or a derivative thereof.

DETAILED DESCRIPTION OF THE INVENTION

[0007] The anthranilic acid or a derivative thereof employed in the invention is represented by the above-mentioned formula (1). In the formula (1), each of R^1, R^2, R^3 and R^4 is the same or different and is a hydrogen atom, a halogen atom, or a group that does not participate in the reaction and may have a substituent. In more detail, each is hydrogen, alkyl, cycloalkyl, aralkyl, aryl, halogen, hydroxyl, alkoxy, alkylthio, nitro, cyano, carbonyl, or amino(not for R^1). Otherwise, R^1, R^2, R^3 and R^4 may be combined to form a ring. The alkyl contained in these groups preferably has 1 to 12 carbon atoms.

[0008] Examples of the alkyl groups include methyl, ethyl, propyl, butyl, pentyl, hexyl, heptyl, octyl, nonyl, and decyl. These groups can be any of isomers. Examples of the cycloalkyl groups include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, and cyclooctyl. Examples of the aralkyl groups include benzyl, phenethyl, and phenylpropyl. These groups can be any of isomers. Examples of the aryl groups include phenyl, p-tolyl, naphthyl, and anthranyl. These groups can be any of isomers. Examples of halogen atoms include fluorine, chlorine, bromine, and iodine. Examples of the alkoxy groups include methoxy, ethoxy, and propoxy. These groups can be any of isomers. Examples of the alkylthio groups include methylthio, ethylthio, and propylthio. These groups can be any of isomers.

[0009] The above-mentioned alkyl, cycloalkyl, aralkyl, aryl, alkoxy, alkylthio, and amino(not for R^1) may have a substituent. Examples of the substituents include a substituent bonded via a carbon atom, a substituent bonded via an oxygen atom, a substituent bonded via a nitrogen atom, a substituent bonded via a sulfur atom, and a halogen atom.

[0010] Examples of the substituents bonded via a carbon atom include alkyl groups such as methyl, ethyl, propyl, butyl, pentyl, and hexyl; cycloalkyl groups such as cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl; alkenyl groups such as vinyl, allyl, propenyl, cyclopropenyl, cyclobutenyl, and cyclopentenyl; heterocyclic alkenyl groups such as pyrrolidinyl, pyrrolyl, furyl, and thienyl; aryl groups such as phenyl, tolyl, xylyl, biphenylyl, naphthyl, anthryl, and phenanthoryl; acyl groups (may be acetallized) such as formyl, acetyl, propionyl, acryloyl, pivaloyl, cyclohexylcarbonyl, benzoyl, naphthoyl, and toluoyl; carboxyl groups; alkoxycarbonyl groups such as methoxycarbonyl and ethoxycarbonyl; aryloxycarbonyl groups such as phenoxycarbonyl; halogenated alkyl groups such as trifluoromethyl; and cyano group. These groups can be any of isomers.

[0011] Examples of the substituents bonded via an oxygen atom include hydroxyl; alkoxy groups such as methoxy, ethoxy, propoxy, butoxy, pentyloxy, hexyloxy, heptyloxy, and benzyloxy; and aryloxy groups such as phenoxy, toluyloxy, and naphthyloxy. These groups can be any of isomers.

[0012] Examples of the substituents bonded via a nitrogen atom include primary amino groups such as methylamino, ethylamino, butylamino, cyclohexylamino, phenylamino, and naphthylamino; secondary amino groups such as dimethylamino, diethylamino, dibutylamino, methylethylamino, methylbutylamino, and diphenylamino; heterocyclic amino groups such as morpholino, piperidino, piperazinyl, pyrazolidinyl, pyrrolidino, and indolyl; and imino group. These groups can be any of isomers.

[0013] Examples of the substituents bonded via a sulfur atom include mercapto; thioalkoxy groups such as thiomethoxy, thioethoxy, and thiopropoxy; and thioaryloxy groups such as thiophenoxy, thiotoluyloxy, and thionaphthyloxy. These

groups can be any of isomers.

[0014] Examples of the halogen atoms include fluorine, chlorine, bromine, and iodine.

[0015] The ammonium anthranilate and its derivatives employable in the invention are represented by the aforementioned formula (3). R^1, R^2, R^3 and R^4 seen in the formula (3) have the same meanings as described hereinbefore.

[0016] Examples of the formic acid and its derivatives include formic acid; formic acid esters such as methyl formate and ethyl formate; and orthoformic acid esters such as methyl orthoformate and ethyl orthoformate. Preferred are formic acid esters and orthoformic acid esters. More preferred are orthoformic acid esters. Specifically preferred are methyl orthoformate and ethyl orthoformate.

[0017] The formic acid or its derivatives can be preferably employed in an amount of 1.0 to 10 moles, more preferably 1.1 to 3.0 moles, per one mole of anthranilic acid or its derivatives or ammonium anthranilate or its derivatives.

[0018] The ammonia employed in the reaction can be liquid ammonia or gaseous ammonia. Preferred is a solution of ammonia in an organic solvent such as alcohol (e.g., methanol) and ether (e.g., dioxane). In the latter case, the ammonia solution is of a concentration of, preferably, 1 to 90 wt.%, more preferably 3 to 30 wt.%. The ammonia is preferably employed in an amount of 1 to 60 moles, more preferably 2 to 20 moles, per one mole of anthranilic acid or its derivative.

[0019] The reaction of the invention can be conducted in the presence or absence of a solvent. There are no limitation with respect to the solvents employed in the reaction, provided that the solvents do not disturb the reaction. Examples are alcohols such as methanol, ethanol, isopropyl alcohol, n-butyl alcohol, and t-butyl alcohol; amides such as N,N-dimethylformamide and N-methylpyrrolidone; ureas such as N,N'-dimethylimidazolidinone; sulfoxides such as dimethyl sulfoxide; aromatic hydrocarbons such as benzene, toluene, xylene, and mesitylene; halogenated aliphatic hydrocarbons such as methylene chloride, chloroform, and dichloroethane; nitriles such as acetonitrile and propionitrile; and ethers such as diethyl ether, tetrahydrofuran, and dioxane. Preferred are alcohols. More preferred are methanol and ethanol. These solvents can be employed singly or in combination.

[0020] The amount of the solvent employed in the reaction depends on the homogeneity and stirring condition of the reaction mixture. It is preferred that the solvent is employed in an amount of 0 to 50 g (more preferably 0 to 20 g, most preferably 0 to 5 g) per one gram of the anthranilic acid or its derivative or ammonium anthranilate or its derivative.

[0021] The reaction of the invention can be performed, for instance, by mixing and stirring the compounds to be involved in the invention. The reaction is preferably performed at a temperature of 40 to 200°C, more preferably 50 to 150°C. There is no limitation with respect to the pressure for the reaction.

[0022] After the reaction is complete, the final product, i.e., quinazolin-4-one or its derivative, can be isolated and purified by the conventional procedures such as concentration, distillation, recrystallization, and column chromatography.

[0023] The invention is further described by the following examples.

[Example 1] --- Preparation of quinazolin-4-one

[0024] In a 2-mL volume stainless steel pressure-resistant vessel were placed 260 mg (1.9 mmol) of anthranilic acid, 403 mg (3.8 mmol) of methyl orthoformate, and 1.2 mL (8.4 mmol) of 15 wt.% ammonia methanol solution. The reaction was carried out at 120°C for 2 hours. After the reaction was complete, the reaction mixture was cooled to room temperature and analyzed (according to absolute quantitative analysis) by high performance liquid chromatography. There was produced 278 mg (reaction yield: 100%) of quinazolin-4-one.

[Example 2] --- Preparation of 7-chloroquinazolin-4-one

[0025] In a 2-mL volume stainless steel pressure-resistant vessel were placed 330 mg (1.9 mmol) of 4-chloroanthranilic acid, 403 mg (3.8 mmol) of methyl orthoformate, and 1.2 mL (8.4 mmol) of 15 wt.% ammonia methanol solution. The reaction was carried out at 120°C for 2 hours. After the reaction was complete, the reaction mixture was cooled to room temperature and analyzed (according to absolute quantitative analysis) by high performance liquid chromatography. There was produced 343 mg (reaction yield: 99%) of 7-chloroquinazolin-4-one.

[Example 3] --- Preparation of 6-iodoquinazolin-4-one

[0026] In a 2-mL volume stainless steel pressure-resistant vessel were placed 500 mg (1.9 mmol) of 5-iodoanthranilic acid, 403 mg (3.8 mmol) of methyl orthoformate, and 1.2 mL (8.4 mmol) of 15 wt.% ammonia methanol solution. The reaction was carried out at 120°C for 2 hours. After the reaction was complete, the reaction mixture was cooled to room temperature and analyzed (according to absolute quantitative analysis) by high performance liquid chromatography. There was produced 515 mg (reaction yield: 99%) of 6-iodoquinazolin-4-one.

[Example 4] --- Preparation of 6-iodoquinazolin-4-one

[0027] The procedures of Example 3 were repeated except that the reaction temperature and reaction period were changed to 95°C and 4 hours, respectively. There was produced 485 mg (reaction yield: 93%) of 6-iodoquinazolin-4-one.

[Example 5] --- Preparation of 6-iodoquinazolin-4-one

[0028] The procedures of Example 3 were repeated except that the amount of methyl orthoformate was changed to 320 mg (3.0 mmol). There was produced 514 mg (reaction yield: 99%) of 6-iodoquinazolin-4-one.

[Example 6] --- Preparation of 6-iodoquinazolin-4-one

[0029] In a 200 mL volume stainless steel pressure-resistant vessel equipped with a thermometer, an pressure gauge, and a stirrer were placed 25.0 g (95 mmol) of 5-iodoanthranilic acid, 17.1 g (162 mmol) of methyl orthoformate, and 50 mL (349 mmol) of 15 wt.% ammonia methanol solution. The reaction was carried out at a temperature of 100-110°C and a pressure of 0.5 MPa (gauge pressure) for 8 hours. After the reaction was complete, the reaction mixture was cooled to a temperature of 0-10°C and placed under reduced pressure to distill ammonia off. The residual reaction mixture was then stirred at 0°C for one hour. The precipitated solid was collected by filtration and dried, to obtain 24.3 g (isolated yield: 94%) of 6-iodoquinazolin-4-one as a pale gray crystalline product.

[Example 7] --- Preparation of 6-iodoquinazolin-4-one

[0030] In a 2-mL volume stainless steel pressure-resistant vessel were placed 500 mg (1.9 mmol) of 5-iodoanthranilic acid, 342 mg (5.7 mmol) of methyl formate, and 1.2 mL (8.4 mmol) of 15 wt.% ammonia methanol solution. The reaction was carried out at 150°C for 4 hours. After the reaction was complete, the reaction mixture was cooled to room temperature and analyzed (according to absolute quantitative analysis) by high performance liquid chromatography. There was produced 401 mg (reaction yield: 77%) of 6-iodoquinazolin-4-one.

[Example 8] --- Preparation of 6-iodoquinazolin-4-one

[0031] The procedures of Example 7 were repeated except that methyl formate was changed to 263 mg (5.7 mmol) of formic acid. There was produced 302 mg (reaction yield: 58%) of 6-iodoquinazolin-4-one.

[Reference Example 1] --- Preparation of ammonium anthranilate

[0032] In a 50 mL volume glass vessel equipped with a stirrer and a thermometer were placed 5.0 g (36.5 mmol) of anthranilic acid and 20 mL (156 mmol) of 15 wt.% ammonia methanol solution. The reaction was carried out for 2 hours at room temperature. After the reaction was complete, the reaction mixture was concentrated under reduced pressure, to obtain 5.0 g (isolated yield: 94%) of ammonium anthranilate as white solid.

[0033] The physical characteristics of the ammonium anthranilate were described below.

m.p. (sublimation) : 145 to 146°C

^{1}H-NMR (DMSO-d_6, δ (ppm)): 6.37-6.43 (1H, m), 6.56 (1H, dd, J=1.2, 8.1Hz), 6.95 (6H, brs), 6.98-7.04 (1H, m), 7.69-7.72 (1H, dd, J=1.8, 7.8Hz).

[Example 9 --- Preparation of quinazolin-4-one

[0034] In a 2-mL volume stainless steel pressure-resistant vessel were placed 280 mg (1.8 mmol) of ammonium anthranilate (prepared in the same manner as in Reference Example 1), 400 mg (3.6 mmol) of methyl orthoformate, and 1.5 mL of methanol. The reaction was carried out at 120°C for 2 hours. After the reaction was complete, the reaction mixture was cooled to room temperature and analyzed (according to absolute quantitative analysis) by high performance liquid chromatography. There was produced 214 mg (reaction yield: 81%) of quinazolin-4-one.

[Reference Example 2] --- Preparation of ammonium 4-chloroanthranilate

[0035] In a 50 mL volume glass vessel equipped with a stirrer and a thermometer were placed 5.0 g (29.1 mmol) of 4-chloroanthranilic acid and 20 mL (156 mmol) of 15 wt.% ammonia methanol solution. The reaction was carried out for 2 hours at room temperature. After the reaction was complete, the reaction mixture was concentrated under reduced pressure, to obtain 5.0 g (isolated yield: 95%) of ammonium 4-chloroanthranilate as white solid.

[0036] The physical characteristics of the ammonium 4-chloroanthranilate (which was a new compound) were described below.

m.p. (sublimation): 232 to 233°C

^{1}H-NMR (DMSO-d_6, δ (ppm)): 6.43 (1H, dd, J=2.4, 8.4Hz), 6.69 (1H, d, J=2.4Hz), 7.0 (3H, brs), 7.69 (1H, d, J=8.4Hz), 11.0 (3H, brs).

[Example 10 --- Preparation of 7-chloroquinazolin-4-one

[0037] In a 2-mL volume stainless steel pressure-resistant vessel were placed 340 mg (1.8 mmol) of ammonium 4-chloroanthranilate (prepared in the same manner as in Reference Example 2), 400 mg (3.6 mmol) of methyl orthoformate, and 1.5 mL of methanol. The reaction was carried out at 120°C for 2 hours. After the reaction was complete, the reaction mixture was cooled to room temperature and analyzed (according to absolute quantitative analysis) by high performance liquid chromatography. There was produced 176 mg (reaction yield: 54%) of 7-chloroquinazolin-4-one.

[Reference Example 3] --- Preparation of ammonium 5-chloroanthranilate

[0038] In a 50 mL volume glass vessel equipped with a stirrer and a thermometer were placed 5.0 g (29.1 mmol) of 5-chloroanthranilic acid and 20 mL (156 mmol) of 15 wt.% ammonia methanol solution. The reaction was carried out for 2 hours at room temperature. After the reaction was complete, the reaction mixture was concentrated under reduced pressure, to obtain 5.0 g (isolated yield: 95%) of ammonium 5-chloroanthranilate as pale yellow solid.

[0039] The physical characteristics of the ammonium 5-chloroanthranilate (which was a new compound) were described below.

m.p. (sublimation): 161 to 162°C

^{1}H-NMR (DMSO-d_6, δ (ppm)): 6.57 (1H, d, J=8.4Hz), 6.99 (1H, dd, J=2.7, 8.4Hz), 7.0 (3H, brs), 7.65 (1H, d, J=2.7Hz), 11.0 (3H, brs).

[Example 11 --- Preparation of 6-chloroquinazolin-4-one

[0040] In a 2-mL volume stainless steel pressure-resistant vessel were placed 340 mg (1.8 mmol) of ammonium 5-chloroanthranilate (prepared in the same manner as in Reference Example 3), 400 mg (3.6 mmol) of methyl orthoformate, and 1.5 mL of methanol. The reaction was carried out at 120°C for 2 hours. After the reaction was complete, the reaction mixture was cooled to room temperature and analyzed (according to absolute quantitative analysis) by high performance liquid chromatography. There was produced 307 mg (reaction yield: 94%) of 6-chloroquinazolin-4-one.

[Example 12 --- Preparation of 6-chloroquinazolin-4-one

[0041] In a 2-mL volume stainless steel pressure-resistant vessel were placed 340 mg (1.8 mmol) of ammonium 5-chloroanthranilate (prepared in the same manner as in Reference Example 3), 400 mg (3.6 mmol) of methyl orthoformate, and 1.5 mL of acetonitrile. The reaction was carried out at 120°C for 2 hours. After the reaction was complete, the reaction mixture was cooled to room temperature and analyzed (according to absolute quantitative analysis) by high performance liquid chromatography. There was produced 303 mg (reaction yield: 93%) of 6-chloroquinazolin-4-one.

[Reference Example 4] --- Preparation of ammonium 5-iodoanthranilate

[0042] In a 200 mL volume glass vessel equipped with a stirrer and a thermometer were placed 10.0 g (38 mmol) of 5-iodoanthranilic acid and 100 mL (780 mmol) of 15 wt.% ammonia methanol solution. The reaction was carried out for 3 hours at room temperature. After the reaction was complete, the reaction mixture was concentrated under reduced pressure, to obtain 9.0 g (isolated yield: 85%) of ammonium 5-iodoanthranilate as pale red solid.

[0043] The physical characteristics of the ammonium 5-iodoanthranilate (which was a new compound) were described below.

m.p. (decomposition): 160°C

^{1}H-NMR (DMSO-d_6, δ (ppm)): 6.45 (1H, d, J=8.7Hz), 6.5 (3H, brs), 7.25 (1H, dd, J=2.4, 8.7Hz), 7.96 (1H, d, J=2.4Hz), 11.0 (3H, brs).

[Example 13 --- Preparation of 6-iodoquinazolin-4-one

[0044] In a 2-mL volume stainless steel pressure-resistant vessel were placed 530 mg (1.9 mmol) of ammonium 5-iodoanthranilate (prepared in the same manner as in Reference Example 4), 403 mg (3.8 mmol) of methyl orthoformate, and 1.5 mL of methanol. The reaction was carried out at 120°C for 2 hours. After the reaction was complete, the reaction mixture was cooled to room temperature and analyzed (according to absolute quantitative analysis) by high performance liquid chromatography. There was produced 402 mg (reaction yield: 77%) of 6-iodoquinazolin-4-one.

[Example 14 --- Preparation of 6-iodoquinazolin-4-one

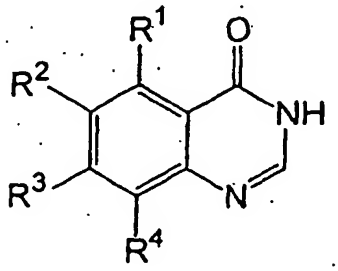
[0045] In a 2-mL volume glass vessel equipped with a reflux condenser were placed 530 mg (1.9 mmol) of ammonium 5-iodoanthranilate (prepared in the same manner as in Reference Example 4), 403 mg (3.8 mmol) of methyl orthoformate, and 1.5 mL of n-butyl alcohol. The reaction was carried out at 120°C for 2 hours. After the reaction was complete, the reaction mixture was cooled to room temperature and analyzed (according to absolute quantitative analysis) by high performance liquid chromatography. There was produced 350 mg (reaction yield: 67%) of 6-iodoquinazolin-4-one.

UTILIZATION IN INDUSTRY

[0046] According to the invention, quinazolin-4-one or its derivative can be prepared from anthranilic acid or its derivatives or ammonium anthranilate or its derivative in a high yield under moderate conditions by simple procedures.

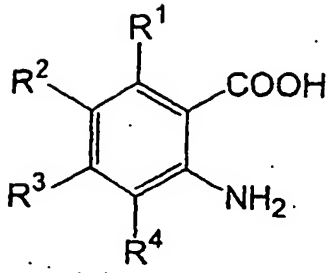
Claims

1. A process for preparing quinazolin-4-one or a derivative thereof having the formula (2):



(2)

in which each of R^1, R^2, R^3 and R^4 independently represents a hydrogen atom, a halogen atom, or a group that does not participate in the following reaction and may have a substituent, or R^1, R^2, R^3 and R^4 may be combined to form a ring,
which is **characterized in that** an anthranilic acid or a derivative thereof having the formula (1):



(1)

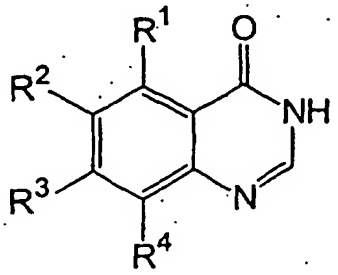
in which each of R^1, R^2, R^3 and R^4 has the same meaning as above,
is reacted with formic acid or a derivative thereof in the presence of ammonia.

2. The process for preparing quinazolin-4-one or a derivative thereof according to claim 1, wherein the anthranilic acid or a derivative thereof is reacted with an orthoformic acid ester.

3. The process for preparing quinazolin-4-one or a derivative thereof according to claim 1, wherein each of R^1, R^2, R^3 and R^4 independently is a hydrogen atom or a halogen atom.

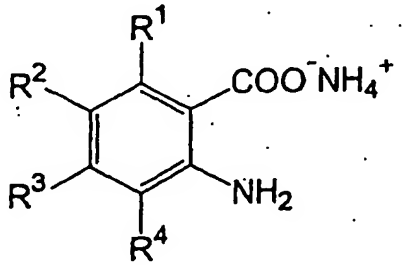
4. The process for preparing quinazolin-4-one or a derivative thereof according to claim 1, wherein each of R^1, R^2, R^3 and R^4 independently is a hydrogen atom, a halogen atom, or a group selected from the group consisting of alkyl, cycloalkyl, aralkyl, aryl, hydroxyl, alkoxy, alkylthio, nitro, cyano, carbonyl, and amino, provided that R^1 is not amino.

5. A process for preparing quinazolin-4-one or a derivative thereof having the formula (2):



(2)

in which each of R^1, R^2, R^3 and R^4 independently represents a hydrogen atom, a halogen atom, or a group that does not participate in the following reaction and may have a substituent, or R^1, R^2, R^3 and R^4 may be combined to form a ring,
which is **characterized in that** ammonium anthranilate or a derivative thereof having the formula (3):



(3)

in which each of R^1, R^2, R^3 and R^4 has the same meaning as above,

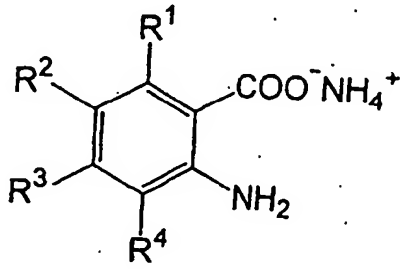
is reacted with formic acid or a derivative thereof.

6. The process for preparing quinazolin-4-one or a derivative thereof according to claim 5, wherein the ammonium anthranilate or a derivative thereof is reacted with an orthoformic acid ester.

7. The process for preparing quinazolin-4-one or a derivative thereof according to claim 5, wherein each of R^1, R^2, R^3 and R^4 independently is a hydrogen atom or a halogen atom.

8. The process for preparing quinazolin-4-one or a derivative thereof according to claim 5, wherein each of R^1, R^2, R^3 and R^4 independently is a hydrogen atom, a halogen atom, or a group selected from the group consisting of alkyl, cycloalkyl, aralkyl, aryl, hydroxyl, alkoxy, alkylthio, nitro, cyano, carbonyl, and amino, provided that R^1 is not amino.

9. Ammonium anthranilate or a derivative thereof having the formula (3):



(3)

wherein each of R^1, R^2, R^3 and R^4 independently is a hydrogen atom, a halogen atom, or a group selected from the group consisting of alkyl, cycloalkyl, aralkyl, aryl, hydroxyl, alkoxy, alkylthio, nitro, cyano, carbonyl, and amino, provided that R^1 is not amino, and that there is no case that all of R^1, R^2, Rand R^4 are hydrogen.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP02/13321

A. CLASSIFICATION OF SUBJECT MATTER
Int.Cl[7] C07D239/88, C07C229/56

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
Int.Cl[7] C07D239/88, C07C229/56

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
CA(STN), REGISTRY(STN), WPIDS(STN)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	JP 9-508126 A (Warner-Lambert Co.), 19 August, 1997 (19.08.97), Page 95 & WO 95/19970 A	1-8
X	Bergman, Jan; Bergman, Solveig; Brimert, Thomas, Syntheses of gem-dinitro heterocyclic compounds, their ring-opening reactions and transformations into indoles, indazoles, and benzoxazinones, Tetrahedron (1999), 55(34), 10447-10466	9
X	Brzyska, W.; Borzechowski, K., Preparation, properties and thermal decomposition of Y(III) and lanthanide(III) complexes with 2-amino-5-chlorobenzoic acid, Polish Journal of Chemistry (1997), 71(11), 1518-1524	9

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier document but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
03 February, 2003 (03.02.03)	18 February, 2003 (18.02.03)
Name and mailing address of the ISA/ Japanese Patent Office	Authorized officer
Facsimile No.	Telephone No.

Form PCT/ISA/210 (second sheet) (July 1998)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP02/13321

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Mrozek, R.; Sikorska, M.; Rzaczynska, Z., Thermal decomposition of rare earth complexes with 2-amino-3, 5-dichlorobenzoic acid, Synthesis and Reactivity in Inorganic and Metal-Organic Chemistry (1997), 27(5), 707-720	9
X	JP 61-52277 A (Showa Denko Kabushiki Kaisha), 14 March, 1986 (14.03.86), Example 2 (Family: none)	9

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP02/13321

Box I Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.: 1-9
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
(See extra sheet)

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest
☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

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INTERNATIONAL SEARCH REPORT

International application No.
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Continuation of Box No.I-2 of continuation of first sheet(1)

The term "derivative" used in the claims is unclear as to what structure is implied, even when the statements in the description are investigated. This term hence makes the scope of the production processes and compounds of the invention unclear.

Consequently, claims 1-9 and the description do not comply with the given requirements to such a degree that a meaningful international search can be made.

In this international search report, a search was hence made through prior art documents with respect to the compounds specified in the description.

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